# Chapter 1

**Answers to Exercises**

* 1. (a) Ka = 3290 M-1. Error = ± 5 %.

(b) Method = Nelder-Mead, K11 = 18300 M-1, error = ± 14 %; K12 = 848 M-1, error = ± 14 %.

Method = L-BFGS-B. K11 = 3670 M-1, error = ± 5 %; K12 = 2.75 x 10-8 M-1, error = ± 47 %.

(c) The most likely binding stoichiometry is 1:1. Based on the shape of the 1:1 binding isotherm obtained in (a) (see Figure 1.21 below), binding is reasonably strong, and hence a Ka value of c.a. 3000 M-1 is not implausible. Furthermore, the error obtained is < ± 10 %, and hence rather small. The fit curve also passes through almost all of the empirical data points, indicating a good fit with experiment. For (b), the errors obtained using the Nelder-Mead method are significantly larger, and K11 is far too large to match the observations. If K11 = 18300 M-1 were to be correct, saturation of the binding isotherm at around 1.0 equivalent of guest should be observed, which is not the case in reality. Using the ‘L-BFGS-B’ method gives more realistic K11 values, but the value of K12 is so small as to be almost negligible. Thus, it may still be safely concluded that this pair of host and guest molecules form a 1:1 stoichiometric host-guest complex in solution.



**Figure 1.21.** Host-guest 1:1 stoichiometric binding curve. Filled circles = empirical data points and the continuous line represents the line of best-fit obtained from non-linear regression.

(d) From the equation ln*K*a = - $\frac{ΔG}{RT}$ (rearrangement of equation 1.5), it is clear that the magnitude of the binding constant is temperature-dependent. Hence, reporting binding constants without the temperature is essentially meaningless.

* 1. The host-guest complex is in slow exchange on the NMR timescale and hence the areas under the host-guest (HG) peak and the free host (H) gives their equilibrium molar ratio. Assuming no complexation, the initial concentrations of the host (H) and guest (G) are 1.5 mM and 1.8 mM respectively. After complexation occurs, the complex (HG) and host are present in a 3.6:1.0 mole ratio by NMR integration. Therefore, the final equilibrium concentration of host = 1/(1+3.6) x 1.5 mM = 0.33 mM, and that of the HG complex is 3 x 0.33 mM = 0.99 mM. Hence, (1.50 – 0.33) = 1.17 mM of host was consumed in forming the complex. Since 1 equivalent of guest is consumed per equivalent of host in complex formation, the final guest concentration at equilibrium is (1.80 – 1.17) = 0.63 mM. Substituting [H] = 0.33 mM, [G] = 0.63 mM and [HG] = 0.99 mM into the equilibrium equation Ka = [HG]/([H][G]), Ka works out to be 0.00099/ (0.00033 x 0.00063) = 4762 M-1 = 4800 M-1 (correct to 2 significant figures).
	2. (a) $K\_{1}= \frac{[HG]}{\left[H\right][G]}$ and $K\_{2}= \frac{[HG\_{2}]}{\left[HG\right][G]}$

(b) Rearrange the expression for *K*1 such that [HG] = *K*1[H][G]. Substitute this expression into that of *K*2 in (a): $K\_{2}= \frac{[HG\_{2}]}{(K\_{1}[H][G])[G]}$ $= \frac{[HG\_{2}]}{K\_{1}\left[H\right][G]^{2}}$

(c) By definition, β12 = *K*1*K*2. Substitute the expressions for *K*1 and *K*2 in (a) into this equation to obtain: β12 = $\left(\frac{[HG]}{\left[H\right][G]}\right)\left(\frac{[HG\_{2}]}{\left[HG\right][G]}\right)$ = $\frac{[HG\_{2}]}{\left[H\right][G]^{2}}$.